e-ISSN: 0975-5160, p-ISSN: 2820-2651

Available online on www.ijtpr.com

International Journal of Toxicological and Pharmacological Research 2023; 13 (12); 105-109

Original Research Article

Carbetocin versus Oxytocin for the Prevention of Postpartum Hemorrhage

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Received: 18-09-2023 / Revised: 21-10-2023 / Accepted: 26-11-2023
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Conflict of interest: Nil

Abstract:

Background and Aim: Carbetocin and oxytocin are prescribed for the purpose of preventing uterine atony-induced postpartum haemorrhage (PPH). A more recent substitute for oxytocin, carbetocin has a prolonged half-life and is more resistant to heat. Reduced PPH can be achieved through the preventative administration of uterotonics. Comparing the effects of oxytocin and carbetocin on placental separation, blood loss control, and the amount of additional uterotonic required during caesarean section (CS) in patients at high risk for primary PPH were the objectives of the present study.

Material and Methods: One hundred elective CS-undergoing women were recruited for the investigation. They were separated into two groups at random. At delivery of the anterior shoulder, women in the carbetocin group (group A) were administered a bolus of 100 µg IV. Conversely, women in the oxytocin group (group B) were administered 20 IU of oxytocin in 1000 mL of 0.9% NaCl solution IV (at a rate of 150 mL per hour). The effects of carbetocin and oxytocin on blood pressure (BP) at 1 minute and 5 minutes after injection were evaluated in this study. The time required for placental separation, uterine tone, the necessity for supplementary uterotonic agents, and the decrease in haemoglobin level as determined by comparing the concentration of haemoglobin at admission and 24 hours postpartum, as well as the visual assessment of blood loss, were also evaluated and compared.

Results: The oxytocin group exhibited early placental separation in 73% of patients (less than 30 seconds), whereas the carbetocin group demonstrated placental separation after more than one minute. In both research groups, haemoglobin levels were comparable before and after 24 hours from the time of delivery. In group A, the median haemoglobin value was 12.1 gm/dl prior to LSCS and 10.9 gm/dl following the procedure. Additionally, uterine tone was observed to increase in the oxytocin group within 30 seconds, whereas it took the carbetocin group 60 seconds to achieve the same result. However, the tone remained constant in the carbetocin group, and group A did not receive any further utero tonics. 45% of patients in the oxytocin group required additional uterotonics (p0.05).

Conclusion: The administration of carbetocin via a single injection offers greater convenience compared to the requirement of a priming injection followed by several hours of oxytocin infusion.

Keywords: Carbetocin, Haemoglobin, Postpartum Haemorrhage, Oxytocin.

Introduction

Notwithstanding the progress achieved in technology over the last few decades, postpartum haemorrhage (PPH) continues to be a significant contributor to maternal mortality in developing countries. [1] Uterine atony is the most prevalent foetal aetiology factor. [2] However, prophylactic use of uterotonics is effective in reducing PPH, with oxytocin being the preferred uterotonic. Oxytocin is secreted into the circulation by the posterior pituitary gland after being produced in the hypothalamus. In addition to stimulating the contraction of the uterine muscles, oxytocin increases prostaglandin production, which further intensifies the contractions. Compared to alternative uterotonics, it exhibits a quicker onset of action and fewer adverse effects, while also reducing the incidence of PPH by 40%. [3-5] It necessitates repetitive intramuscular injections or a continuous intravenous infusion due to its short half-life of 4 to 10 minutes. [6] In recent times, carbetocin, a more recent substitute for oxytocin, has been introduced. It has an approximate half-life of forty minutes and is long-acting; it is also prescribed for the prevention of uterine atony following caesarean section. At this time, Carbetocin's licencing status restricts its use to prophylactic purposes, excluding therapeutic indications and its application in the context of

caesarean sections. In 2012, a Cochrane review accurately hypothesised the evidence supporting the use of carbetocin to prevent PPH; however, since then, a number of further papers have been published. [7-9]

Caesarean delivery is the primary indication for which carbetocin has been suggested, as it is linked to a greater incidence of severe postpartum haemorrhage (PPH) and necessitates invasive second-line therapies three times more frequently than vaginal deliveries. [10] It has been assessed in limited randomised trials and through subjective or post hoc judgement criteria in women who have undergone caesarean sections. With a risk ratio of 0.71, prophylactic carbetocin does not reduce the incidence of PPH > 500 mL in caesarean deliveries, according to a 2018 Cochrane meta-analysis. [11] Notwithstanding these constraints, the number of studies accessible pertaining to this outcome was moderate, as was the grade of the studies. Conversely, there was a substantial reduction in blood loss and the necessity for supplementary uterotonic agents. Furthermore, additional recent meta-analyses suggest that carbetocin exhibits superiority over oxytocin. [12,13]

Carbetocin exerts its effects with both a prolonged onset and duration. A similar level of safety is observed in comparison to oxytocin. [9] Additionally, it retains heat better than oxytocin. [12] Nevertheless, both medications can be delivered through intravenous and intramuscular routes. Comparing the effects of oxytocin and carbetocin on placental separation, blood loss control, and the amount of additional uterotonic required during caesarean section (CS) in patients at high risk for primary PPH were the objectives of the present study.

Material and Methods:

A comparative observational study was undertaken over the course of one year at the Obstetrics and Gynaecology Tertiary Care Teaching Institute of India. One hundred elective CS-undergoing women were recruited for the investigation. They were separated into two groups at random.

One hundred women received carbetocin as part of Group A, while the remaining one hundred received oxytocin as part of Group B. At delivery of the anterior shoulder, women in the carbetocin group (group A) were administered a bolus of 100 µg IV. Conversely, women in the oxytocin group (group B) were administered 20 IU of oxytocin in 1000 mL of 0.9% NaCl solution IV (at a rate of 150 mL per hour). Informed assent was obtained in writing from the women who were to undergo CS. Spinal anaesthesia was administered.

All expectant women who were at term and had multiple pregnancies, a history of CS, uterine fibroids, foetal macrosomia, PPH within the previous hour, or polyhydramnios met the inclusion criteria.

Exclusion criteria for the study included high-risk pregnancies characterised by hypertensive disorders of pregnancy, cardiac disease, renal or hepatic disease, epilepsy, general anaesthesia, and hypersensitivity to carbetocin and oxytocin.

The effects of carbetocin and oxytocin on blood pressure (BP) at 1 minute and 5 minutes after injection were evaluated in this study. Additional parameters that were assessed and contrasted included the duration of placental separation, uterine tone, necessity for supplementary uterotonic agents, reduction in haemoglobin level as determined by comparing the concentration of haemoglobin at admission and 24 hours postpartum and visual estimation of blood loss.

Statistical analysis

Following the compilation and entry of the recorded data into a spreadsheet application (Microsoft Excel 2007), the information was exported to the data editor tab of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). On the basis of their distribution, quantitative variables were described as means and standard deviations or median and interquartile range. The presentation of qualitative variables consisted of counts and percentages. The levels of significance and confidence were established at 5% and 95%, respectively, for every test.

Results

At baseline, the characteristics of both study groups were observed to be comparable. Both groups underwent CS at term gestation or 38 weeks. Indications for elective CS were comparable across all groups; however, polyhydramnios emerged as the predominant indication in group B (Table 1). In relation to their hemodynamic effects, carbetocin and oxytocin are both hypotensive substances. Systolic and diastolic blood pressure was both reduced in the oxytocin group at uterine closure time and five minutes after administration. Early placental separation was observed in 73% of patients treated with oxytocin (less than 30 seconds), whereas in 78% of patients treated with carbetocin, placental separation occurred after more than one minute. As shown in Table 2, there was no significant difference between the two groups regarding the estimated volume of blood loss or the incidence of primary postpartum haemorrhage (>1000 ml). In both research groups, haemoglobin levels were comparable before and after 24 hours from the time of delivery. In group A, the median haemoglobin value was 12.1 gm/dl prior to LSCS and 10.9 gm/dl following the procedure. The median haemoglobin value in group B was 12.5

gm/dl prior to LSCS and 10.5 gm/dl following the procedure, indicating that there was no statistically significant difference in the extent of blood loss ($p \leq 0.05$).

Additionally, uterine tone was observed to increase in the oxytocin group within 30 seconds, whereas it took the carbetocin group 60 seconds to achieve the same result. However, the tone remained constant in the carbetocin group, and group A did not receive any further utero tonics.

45% of patients in the oxytocin group required additional uterotonics (p0.05). (Figure 3)Notwithstanding the absence of significant adverse effects in both study groups, the carbetocin group exhibited a higher incidence of vertigo and vomiting ($p<0.05$).

Table 1: Characteristics of study population

Variables	Group A N (%)	Group B N (%)
Gestational age at delivery	38	38
Fetal macrosomia	10 (20)	6 (12)
History of PPH	6 (12)	5 (10)
Fetal polyhydramnios	9 (18)	24 (48)

Table 2: Comparison of blood loss during and after CS

Blood loss (ml)	Group A (%)	Group B (%)	P value
After delivery of baby			
>1000	5	7	0.02*
500-1000	9	9	
<500	36	34	
After 2 hours of LSCS			
>1000	0	0	0.01*
500-1000	1	2	
<500	49	48	
After 24 hours of LSCS			
>1000	0	0	NA
500-1000	0	0	
<500	0	0	

* indicate statistically significance at $p \leq 0.05$

Table 3: Use of additional uterotonics in both groups

Uterotonics	Group A (%)	Group B (%)
Additional uterotonic used	11	69
Intermittently relaxed uterus	3	57
Sustained uterine contractility	97	42

Discussion

In the current study, the hemodynamic effects and prophylactic effects of carbetocin (group A) and oxytocin (group B) were compared in CSs with risk factors for primary post-partum haemorrhage. The groups' baseline characteristics were similar, and their safety profiles were also similar. Both oxytocin and carbetocin caused hypotension, however oxytocin had a stronger effect. The amount of blood lost following CS and the decrease in haemoglobin level within two and twenty-four hours of LSCS did not differ significantly. Additionally, we saw that the carbetocin group took longer to achieve appropriate uterine tone and placental separation (>1 minute). But once the carbetocin group reached the appropriate tone, it persisted throughout the LSCS. Therefore, this group did not require any further uterotonics. In contrast, the oxytocin group saw early placental separation and the early recovery of normal uterine tone. This uterine tone was not maintained, nevertheless. We employed additional uterotonics to prevent intermittent uterine atony, which was seen in the majority of the patients in this group. The findings of this investigation align with the most current Cochrane review. [14] Similarly, no discernible difference was identified between oxytocin and carbetocin in other investigations that similarly used the change in Hb as an endpoint. [15,16] identical PPH rates were identified in the two arms of a trial involving 635 women and following protocols identical to ours. [17] Carbetocin has been found to be superior in several investigations when the major result was the requirement for extra uterotonics. [15, 17, 18] However, this result is rather arbitrary and does not directly relate to maternal health. Because it depends on the subjective assessment of bleeding and the anticipated risk of the prophylactic injection's failure, the usage of different uterotonics differs greatly amongst obstetricians. The same

disadvantages apply to studies that have selected uterine atony or the requirement for uterine massage as their end points. [13,18]

An intriguing finding revealed that the addition of carbetocin as a uterotonic resulted in prolonged uterine contractions and preserved uterine tone in the oxytocin group. Moreover, there was no placental separation delay observed when both medications were taken together. The use of carbetocin should not be administered in cases of placenta previa, Accreta, pre-eclampsia, eclampsia, or general anaesthesia. In reference to the research on carbetocin, Danzereau et al. initially reported that women who took the medication shortly after giving birth had a decreased requirement for subsequent uterotonic treatment for uterine atony. [12,13,19]

Carbatocin permits the early removal of IV lines, which is a part of current protocols for improved recovery following caesarean deliveries, even if it is not more effective than oxytocin in avoiding PPH.20 Reductions in retreatment, staffing needs, transfusions, and possible medication errors appear to offset the greater initial cost of carbetocin, according to certain cost-benefit evaluations. [21,22] Therefore, carbetocin may be a cost-effective prophylactic treatment against PPH in caesarean deliveries from a pharmacoeconomic standpoint.

Conclusion

The duration of action of carbetocin's prolonged. It results in a prolonged uterine response with more frequent and amplitude contractions. It is more convenient to administer carbetocin injections all at once rather than oxytocin boluses that require several hours of oxytocin infusion afterward. After carbetocin is administered, uterotonics are not used again. On the other hand, it results in delayed placental separation and delayed uterine tone restoration as compared to oxytocin.

It can be administered in place of oxytocin as the main uterotonic agent or as a follow-up uterotonic. While prolonged uterine tone, early placental separation, and the absence of intermittent atony are benefits of combination usage. But if carbetocin is to be given as an extra uterotonic, the oxytocin drip needs to be halted.

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